REMARKS/ARGUMENTS

With this amendment, claims 1-119 are pending. New claims 120-122 are added. For convenience, the Examiner's rejections are addressed in the order presented in a January 29, 2003, Office Action. Certain issues raised in an advisory action mailed June 16, 2003, are also addressed.

I. Status of the claims

Claims 2, 4-7, 10-14, 16-36, 38-40, 42, 44, 53-56, 58, 60-65, 68, 71, 75, 78-83, and 86-116 are cancelled without prejudice to subsequent revival.

Independent claim 1 and dependent claims, independent claim 66, and independent claim 67 and dependent claims are all amended to recite a recombinant gram negative enteric bacterium rather than a recombinant microorganism. Support for these amendments is found throughout the specification, for example, at original claims 82, 83, 104, and 105 and page 23, lines 24-29; and at original claim 56 and page 13, lines 19-21 and page 22, lines 27-28. These amendments add no new matter.

Claims 1, 66, and 67 are also amended to recite that the recombinant bacterium displays a binding moiety that acts as a receptor mimic of a toxin or adhesion of a pathogenic organism. Support for these amendments is found throughout the specification, for example at page 3 line 29 through page 4, line 14 and at page 13, lines 19-21. These amendment add no new matter.

Claims 1, 66, 67, and 117 are also amended to recite that the binding moiety consists of an oligosaccharide that is part of a lipopolysaccharide. Support for these amendments is found throughout the specification, for example at page 32, lines 3-4 and original claims 56, 57, and 87. These amendment add no new matter.

Claim 3 is amended to recite that a second sugar residue is attached to the binding moiety by at least a second glycosyltransferase. Support for this amendment is found throughout the specification, for example at page 4, lines 1-2.

Claims 66 and 67 are amended to recite that one or more exogenous nucleotide sugar precursor synthesizing enzymes are encoded by a second exogenous nucleic acid. Support for these amendments is found throughout the specification, for example, at page 4, line26 through page 5, line 4. These amendments add no new matter. Claims 66 and 67 are also mended to recite that the acceptor molecule is a chimeric carbohydrate molecule that is a lipopolysaccharide. Support for these amendments is found throughout the specification, for example, at page 9, lines 14-16. These amendments add no new matter.

Claim 73 is amended to correct obvious grammatical errors. This amendment adds no new matter.

In response to an Advisory Action mailed June 17, 2003, microorganism is replaced by bacterium in proposed claims 3 and 46. A misspelling is corrected in proposed claim 67. Applicants also believe objections to grammar in proposed claims 66 and 67 are now addressed.

II. Objections to the Specification

At the request of the Examiner, Applicants have amended paragraphs to remove hyperlinks or browser executable code at page 10, line 30; page 32, line 10; page 56, line 28; and page 62, line 28.

III. Rejections under 35 U.S.C. §112, written description

Claims 1-9, 15, 25, 36-37, 41, 43, 45-70, 72-85, 88-91, 97-107, 110 and 117-119 are rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification as originally filed. In the Office Action the Examiner observed that the purpose of the written description requirement is to convey to one skilled in the relevant art that the inventors had possession of the claimed invention as of the filing date.

To the extent the rejection applies to the claims as amended, Applicants respectfully traverse the rejection. Amended claims 1, 66, and 67 now read on a genus of recombinant gram negative enteric bacteria that display a receptor mimic on their surface, wherein the receptor mimic is oligosaccharide that is part of a lipopolysaccharide molecule.

Applicants also respectfully bring to the Examiner's attention that claims117 is directed to recombinant E. coli bacteria that display a receptor mimic on their surface, wherein the receptor mimic is oligosaccharide that is part of a lipopolysaccharide molecule. Dependent claims 118 and 119 recite specific oligosaccharides that act as receptor mimics.

The Examiner alleges that the specification provides description only for use of E. coli in the present invention. Applicants submit that the specification describes a representative number of species that make up the claimed genus of gram negative enteric bacteria. Applicants provide description of the use of both *E. coli* and *Salmonella enterica sv typhimurium* bacteria in the claimed invention. (*See, e.g.*, Example 1 and Table 9, page 47.) Applicants respectfully submit that the disclosure in relation to *S. typhimurium* is by no means cursory or preliminary in nature, and refer particularly to the last three rows of Table 9 where it can be seen that not only has one introduced the exogenous DNA in *S. typhimurium*, and had expression of the gene encoded thereon, but there is data to show that the recombinant *S. typhimurium* bacterium also has neutralizing activity and therefore the LPS thereof comprises a receptor mimic. It is submitted that a person in the present field of endeavour would clearly accept that the inventors have produced a receptor mimic in *S. typhimurium* and also that the present invention is applicable to other bacteria, in particular bacteria that express LPS (that is gram negative bacteria), and are enteric. It is to be noted that reference to enteric bacteria further limits the scope of the claim beyond gram negative to those that are associated with the gastrointestinal tract.

The Office Action alleges that claims directed to microorganisms with reduced production of external masking polysaccharides, to glycosyltransferases that have been mutated to reduce phase variation, and to microorganisms that exhibit enhanced resistance to colicins are not adequately described. In order to expedite prosecution, all claims with the above listed limitations have been cancelled.

The Office Action alleges that the specification provides sufficient guidance only for recombinant gram negative bacteria that have a lipopolysaccharide surface. In order to expedite prosecution, Applicants have amended claims 1, 66, 67, 117 to require a receptor mimic to be part of a lipopolysaccaride acceptor molecule.

In view of the above amendments and remarks, Applicants respectfully request that the rejection under 35 U.S.C. §112, first paragraph, written description, be withdrawn.

IV. Rejections under 35 U.S.C. §112, enablement

Claims 1-9, 15, 25, 36-37, 41, 43, 45-70, 72-85, 88-91, 97-107, 110 and 117-119 are rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement. The test of enablement is "whether one skilled in the art could make or use the claimed invention from the disclosure in the patent coupled with information known in the art without undue experimentation" (*see, e.g.*, MPEP §2164.01).

To the extent the rejection applies to the claims as amended, Applicants respectfully traverse the rejection. Amended claims 1, 66, and 67 now read on a genus of recombinant gram negative enteric bacteria that display a receptor mimic on their surface, wherein the receptor mimic is oligosaccharide that is part of a lipopolysaccharide molecule. Applicants also respectfully bring to the Examiner's attention that claims117 is directed to recombinant *E. coli* bacteria that display a receptor mimic on their surface, wherein the receptor mimic is oligosaccharide that is part of a lipopolysaccharide molecule. Dependent claims 118 and 119 recite specific oligosaccharides that act as receptor mimics.

The Office Action alleges that the claimed genus is not described and that one of skill would not know how to make and use the invention as intended. In response, as indicated above, Applicants submit the claimed genus is fully described and thus, meets the enablement requirement.

The Office Action alleges that the specification enable only the use of *E. coli* in the claimed invention. Applicants disclose the use of both *E. coli* and *Salmonella enterica sv typhimurium* bacteria in the claimed invention. (See, e.g., Example 1 and Table 9, page 47.) Applicants respectfully submit that the disclosure in relation to *S. typhimurium* is by no means cursory or preliminary in nature, and refer particularly to the last three rows of Table 9 where it can be seen that not only has one introduced the exogenous DNA in *S. typhimurium*, and had expression of the gene encoded thereon, but there is data to show that the recombinant *S. typhimurium* bacterium also has neutralizing activity and therefore the LPS thereof comprises a

receptor mimic. It is submitted that a person in the present field of endeavor would clearly accept that the inventors have produced a receptor mimic in *S. typhimurium* and also that the present invention is applicable to other bacteria, in particular bacteria that express LPS (that is gram negative bacteria), and are enteric. It is to be noted that reference to enteric bacteria further limits the scope of the claim beyond gram negative to those that are associated with the gastrointestinal tract.

The Office Action alleges that a lipopolysaccharide is an essential feature of the claimed invention. In order to expedite prosecution, Applicants have amended claims 1, 66, 67, 117 to require a receptor mimic to be part of a lipopolysaccharide acceptor molecule.

The Office Action also alleges that the specification is enabled only for the use of *E. coli* and that use of plasmid species in other bacterial is unpredictable. First Applicants submit that the disclosure teaches how to use another bacterial species, *S. typhimurium*, in the claimed invention. Second, even if some bacterial species are unable to be transformed with a plasmid, claims reading on inoperative embodiments are enabled if the skilled artisan understands how to avoid inoperative embodiments. (*See, In re Cook and Merigold*, 169 USPQ 299, 301 (C.C.P.A. 1971)). In the present application, one of skill would know how to avoid inoperative embodiments and make the claimed recombinant bacteria that express receptor mimics without undue experimentation. Moreover, the present application provides guidance in the form of assays and working examples for making and identifying such recombinant bacteria.

The Office Action alleges that claims encompassing colicin resistant microorganisms, claims encompassing glycosyltransferases modified to stabilize phase variation, and claims encompassing some methods of administration are not enabled. In order to expedite prosecution, Applicants have cancelled claims that include those limitations.

The Office Action alleges that the claims read on receptors of chemical toxins and that such receptors are not enabled. In order to expedite prosecution, Applicants have amended claims 1, 66 and 67 to recite that the toxin is that of a pathogenic microorganism or an adhesion of a pathogenic organism.

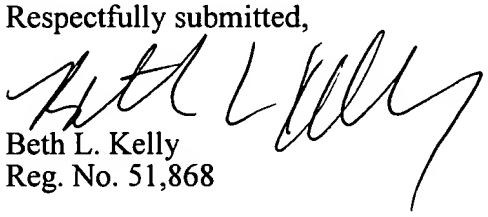
In view of the above amendments and remarks, Applicants respectfully request that the rejection under 35 U.S.C. §112, first paragraph enablement be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



Beth L. Kelly
Reg. No. 51,868

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, 8th Floor
San Francisco, California 94111-3834
Tel: 415-576-0200
Fax: 415-576-0300
BLK:blk
60003719 v1